

Guided Migration of Neural Stem Cells Derived from Human Embryonic Stem Cells by an Electric Field.

Journal:	Stem Cells
Publication Year:	2011
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PubMed link:	22076946
Funding Grants:	Sustained siRNA production from human MSC to treat Huntingtons Disease and other neurodegenerative disorders, Directing migration of human stem cells with electric fields

Public Summary:

It is possible to transplant human embryonic stem cell-derived neurons into the brain of rodents and other animals to test potential treatments and replacement therapies for neurodegenerative diseases and brain damage. However, the implanted cells might not end up in the desired area, where they could best make an impact in treating the damage or replacing lost cells. Dr. Zhao's team studies a mild electrical pulse to guide cells to the area where they are needed. The tiny electrical probe acts rather like the "pied piper" and the cells follow it. The scientific term for this interesting system is "galvanotaxis". This paper reports, for the first time, that human neural stem cells that had been created under defined conditions from the embryonic stem cell line H9 also display this behavior. Associated videos show the cells following the electrical gradient toward the cathode, then when the electrical field is reversed, they flip over like a swimmer in a pool and move in the opposite direction. We are currently studying galvanotaxis in the brains of rodents transplanted with human hESC-derived neurons. It may seem far-fetched to think about electrodes in the brain, but this is a very weak pulse that does not damage surrounding tissue, and it is related to the now standard practice of deep brain stimulation for patients with Parkinson's disease. We hope to guide transplanted neurons and neural stem cells to the area of the brain that most needs repair, through this CIRM-funded research.

Scientific Abstract:

Small direct current (DC) electric fields (EFs) guide neurite growth and migration of rodent neural stem cells. This however could be species dependent. It is therefore critical to investigate how human neural stem cells (hNSCs) respond to EF before any possible clinical attempt. Aiming to characterize the EF-stimulated and guided migration of hNSCs, we derived hNSCs from a well-established human embryonic stem cell line H9. Small applied DC EFs, as low as 16 mV/mm, induced significant directional migration toward the cathode. Reversal of the field polarity reversed migration of hNSCs. The galvanotactic/electrotactic response was both time and voltage dependent. The migration directedness and distance to the cathode increased with the increase of field strength. Rock inhibitor Y27632 is used to enhance viability of stem cells and has previously been reported to inhibit EF-guided directional migration in induced pluripotent stem cells and neurons. Its presence, however, did not significantly affect the directionality of hNSC migration in an EF. Cytokine receptor CXCR4 is important for chemotaxis of NSCs in the brain. The blockage of CXCR4 did not affect the electrotaxis of hNSCs. We conclude that hNSCs respond to a small EF by directional migration. Applied EFs could potentially be further exploited to guide hNSCs to injured sites in the central nervous system to improve the outcome of various diseases.

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